122804

Shaughnessy No.: 122804

Date Out of EAB: AUG 28 1985

To: G. LaRocca
Product Manager 15
Registration Division (TS-767)

From: Samuel M. Creeger, Chief
Review Section #1
Exposure Assessment Branch
Hazard Evaluation Division (TS-769)

Attached, please find the EAB review of...

Reg./File # : 618-OG and-OV

Chemical Name: Avermectin

Type Product : Insecticide

Product Name : AFFIRM

Company Name : Merck

Purpose : New Chemical, Request for Product Registration to Control Fire Ants.

Action Code(s): 120

EAB #(s) : 5820 & 5824

Date Received: 8/2/85

TAIS Code:

Date Completed: AUG 28 1985

Total Reviewing Time: 3.5 days

Deferrals to:

____ Ecological Effects Branch

____ Residue Chemistry Branch

____ Toxicology Branch

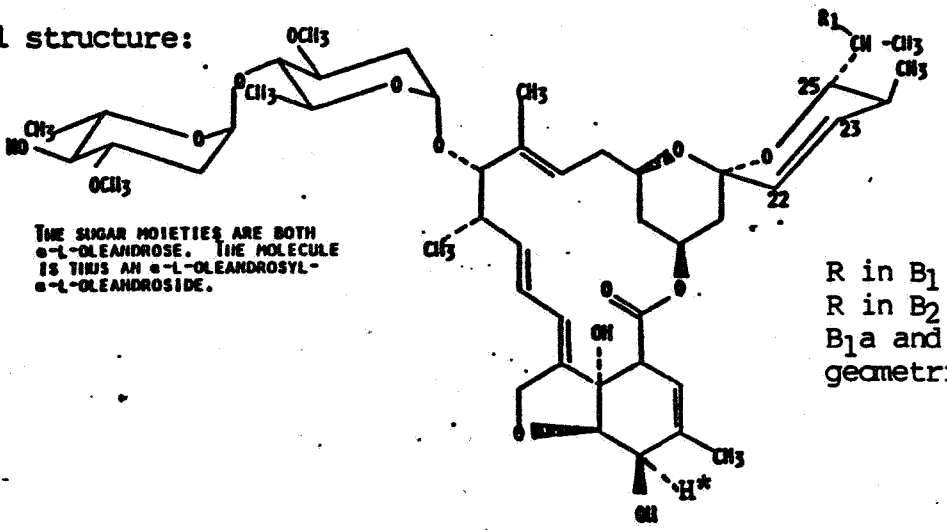
1.a CHEMICAL:

Avermectin B_1

Abamectin.

Common/chemical name: Avermectin (Mk-0936)

Chemical structure:



The acive ingredient is composed of not less than 80% avermectin B_1a and not more than 20% avermectin B_1b.

1.b Physical Properties:

See earlier reports.

2. TEST MATERIAL:

Formulations of Avermectin B_1.

3. STUDY/ACTION TYPE:

Additional data in support of registration of Avermectin B_1 for use as a Fire Ant Insecticide.

4. STUDY IDENTIFICATION:

1. Photolysis Stability of Intermediates Formed During the Photolysis of Avermectin B_1a in Water.

2. Description of the Degradate Fractions Isolated from the Photolysis of Avermectin B_1a and Tested for Acute Toxicity to Daphnia Magna

3. Results of Daphnia Bioassay of MK-0936, Avermectin B_1a Standard, Polar and Non-polar Metabolites from a Water Photolysis Reaction of Avermectin B_1 Standard

4. Stability of VERTIMEC on Petri Dishes under various Light Conditions.

5. Stability of Abamectin Affirm™ Imported Fire Ant Bait Exposed to Natural Sunlight.

5. REVIEWED BY:

Akiva D. Abramovitch, Ph.D.
Chemist
Environmental Chemistry Review Section 1/EAB/HED/OPP Date: / /85

6. APPROVED BY:

Samuel M. Creeger, Chief
Supervisory Chemist
Environmental Chemistry Review Section 1/EAB/HED/OPP Date: / /85

AUG 28 1985

7. CONCLUSIONS:

The aqueous photolysis study was reviewed and found acceptable by the EAB review of March 28, 1984. The additional studies submitted were helpful in demonstrating that both Avermectin B_1a and its geometric isomer B_1b formed during photolysis, degraded under sunlight conditions in aqueous solutions and in AFFIRM bait pellets, with half lives of less than 12 hours.

8. RECOMMENDATIONS:

The statements made by Merck with regard to the low toxicity of the photolysis degradation products of Abamectin should be addressed by EEB particularly since the identity of these degradates remained unknown (refer sections 10.1 E 10.2 E and 10.3 E to EEB). All guidelines data requirements have been satisfied for the proposed fire ant use with the exception of a field dissipation study. However, the field dissipation study is now under review with a separate action.

9. BACKGROUND:

A. Introduction: Merck submitted additional data to support registration of Avermectin B_1 for use as a Fire Ant Insecticide.

B. Directions for Use: Please see attachment of the proposed label of Affirm™.

10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES:

10.1 A. Study Identification: Photolysis Stability of Intermediates Formed During the Photolysis of Avermectin B_1a in Water. Addendum to EPA Accession No. 252115.

B. Materials and Methods:

Reported and reviewed in one of the two Avermectin EAB reports of March 28, 1984.

C. Reported Results:

The March 28, 1984 EAB review reported the photolytic half-life at 3.5-12 hours. One of the proposed photoproducts based on NMR and MS analysis (other degradates remained unknown) was the geometric isomer of avermectin B_1a, B_1b shown in the attached figure 9. The current submission provides the photolysis profile of avermectin B_1a indicating

that avermectin B_1b and the other primary degradates had half lives of similar order of magnitude to the parent avermectin B_1a.

D. Study Author's Conclusions:

The author concluded that the primary degradates of avermectin B_1a underwent degradation at comparable rates to the parent compound and thus were not likely to persist in the environment under photolytic conditions.

E. Reviewer's Discussion and Interpretation of Results:

The study was accepted by the EAB review of March 28, 1984 and the additional statement regarding the fate of the primary degradates are noted. The identity of the secondary degradates (other than the geometric isomers of Avermectin B_1b) was not determined. The remarks concerning the toxicity of these degradates should be addressed by the TB and/or EEB.

10.2 A. Study Identification: Description of the Degradate Fractions Isolated from the Photolysis of Avermectin B_1a and Tested for Acute Toxicity to Daphnia Magna.

B. Materials and Methods:

C. Reported Results:

D. Study Author's Conclusions:

E. Reviewer's Discussion and Interpretation of Study Results:

The submission was read by the reviewer and in his opinion the information should be reported and evaluated by the EEB.

10.3 A. Study Identification: Results of Daphnia Bioassay of MK-0936, Avermectin B_1a Standard, Polar and Non-polar Metabolites from a Water Photolysis Reaction of Avermectin B_1 Standard.

B. Materials and Methods:

C. Reported Results:

D. Study Author's Conclusions:

E. Reviewer's Discussion and Interpretation of Study Results:

As in 10.2 E.

10.4 A. Study Identification: Stability of VERTIMEC on Petri Dishes under Various Light Conditions: The study was conducted at the Merck Sharp & Dohme Research Laboratories, Agricultural Research & Development under the directions of Dr. R. A. Dybas.

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B. Materials and Methods:

A 100 microliter aliquot of VERTIMEC 1.8% emulsifiable concentrate formulation was diluted to 100 ml with distilled water. The resulting solution contained approximately 18 microgram of abamectin per milliliter. A volume of 2 ml of this solution was applied to each of 12 sterilized petri dishes and the water was allowed to evaporate in two hours under fluorescent laboratory lights. Three dishes were analyzed immediately, three dishes were left in the dark as controls, three dishes were left on the bench top exposed to the laboratory fluorescent light and the remaining dishes were exposed to radiation from a Sears 275W sunlamp through a pyrex glass. Each glass was washed with 3x5 ml of methylene chloride, the methylene chloride was evaporated and the residue was then redissolved in HPLC grade acetonitrile and analyzed by HPLC.

C. Reported Results:

O time: 15.35 microgram/ml
All values reported in microgram/ml

	DARK	FLUORESCENT LIGHT	SUNLAMP
4 hrs.	14.98	11.08	10.41
7 hrs.	14.62	6.11	2.57
24 hrs.	11.05	2.14	0.31

D. Study Author's Conclusions:

No additional conclusions.

E. Reviewer's Discussions and Interpretation of Study Results:

The light intensity and frequency was not reported and/or shown to be comparable to that of sunlight. However, the photolysis data requirements have already been satisfied (see the March 28, 1984 EAB review).

10.5 A. Study Identification: Stability of Abamectin Affirm™ Imported Fire Ant Bait Exposed to Natural Sunlight. The study was conducted at the Merck Sharp & Dohme Research Laboratories, Agricultural Research & Development under the directions of Dr. R. A. Dybas.

B. Materials and Methods:

AFFIRM baits containing [redacted] abamectin and [redacted] were prepared and stored in the dark at 4°C. The petri dishes were cleaned with freshly prepared chromic acid solution, thorougly washed and sterilized prior to use. The bait (2.0 gm) was spread on the petri dish in a reasonably uniform layer. The following morning the samples were exposed to the sun at 9:00 and the temperatures of the surface recorded periodically with a mercury thermometer. The samples were removed at night and during poor weather conditions and stored in a refrigerator. Under these storage conditions in darkness, AFFIRM [redacted] is known to be stable for at least two years. For analysis,

the bait samples were washed off the plates with methylene chloride, filtered through celite and concentrated. The [redacted] was then applied to a dry silica gel Sep-Pak cartridge. Abamectin was eluted into a clean 50 ml RB flask and analyzed on HPLC. The amounts of Avermectin B_1a and Avermectin B_1b were determined in reference to authentic standards. The temperatures and the light intensity were measured periodically and recorded and were attached to the report.

C. Reported Results:

The amounts of avermectin B_1a & B_1b after various time lengths of solar exposure were as follows:

Time	Solar Exposure	B_1b	B_1a	Total	% Remaining
0 hrs.	0 mWh/cm²	7.2 ppm 7.5	93.3 ppm 98.3	101 ppm 106	(100%)
4 hrs.	323	6.1 7.8	78.5 95.0	84.6 103	90.6%
8 hrs.	572	5.7 5.5	66.0 66.1	71.7 71.6	69.2%
12 hrs.	909	3.2 4.3 4.7	41.6 46.8 44.0	44.8 51.1 48.7	46.6%
16 hrs.	1138	3.4 1.7 3.3	35.3 30.1 31.9	38.7 31.8 35.3	34.1%
23 hrs.	1693 mWh/cm²	1.4 ppm 1.5 1.5	21.0 ppm 21.1 17.8	22.4 ppm 22.6 19.3	20.7%
30 hrs.	2100	1.2 1.2 N.D.* N.D.	13.9 13.5 11.1 11.1	15.1 14.9 11.1 11.1	12.7%

*N.D. = not detected (peak area was below reject value).

D. Study Author's Conclusions:

The author concluded that the initial half life was about 850 mWh/cm^2 which corresponded to about 10-12 hours of a clear summer day sunshine exposure (a full day corresponds to 650-750 mWh/cm^2). The decomposition rate under sunlight condition was several orders of magnitude larger than the rate observed in the dark, indicating that photolysis is a very important degradation pathway for abamectin.

E. Reviewer's Discussions and Interpretation of Study Results:

The study provided valuable information with regard to the rate of disappearance of Avermectin B_1a and B_1b in AFFIRM baits under sunlight conditions. However, the data did not identify the degradation products of Avermectin B_1a or provide an explanation for the unaccounted residues. However, the photolysis data requirements have already been satisfied (see the March 28, 1984 EAB review).

11. COMPLETION OF ONE LINER:

Not completed.

12. CBI APENDIX:

None

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Avermectin science review

Page _____ is not included in this copy.

Pages 8 through 12 are not included in this copy.

The material not included contains the following type of information:

___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

___ A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

X FIFRA registration data

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